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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/664,668	09/18/2003	James McSwiggen	MBHB02-742-E (400/130)	5711
65778 7590 12/31/2007 MCDONNELL, BOEHNEN, HULBERT AND BERGHOFF, LLP 300 SOUTH WACKER DRIVE SUITE 3100 CHICAGO, IL 60606			EXAMINER GIBBS, TERRA C	
			ART UNIT 1635	PAPER NUMBER
			MAIL DATE 12/31/2007	DELIVERY MODE PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/664,668	Applicant(s) MCSWIGGEN ET AL.	
	Examiner Terra C. Gibbs	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 February 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-30 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 18 September 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>See Continuation Sheet</u> . | 6) <input type="checkbox"/> Other: _____ |

Continuation of Attachment(s) 3). Information Disclosure Statement(s) (PTO/SB/08), Paper No(s)/Mail Date :5/31/07, 11/2/06, 10/13/05, 7/22/04.

DETAILED ACTION

This Office Action is a response to Applicant's Preliminary Amendment filed February 26, 2004.

Claims 31-36 have been canceled. Claims 1, 8, 10, and 18 have been amended.

Claims 1-30 are pending in the instant application.

Claims 1-30 have been examined on the merits.

Withdrawal of Previous Office Action

The previous Notice of Non-Compliant Amendment mailed September 25, 2007 is withdrawn. It is noted that this Notice was sent in error because the Examiner indicated that claim 8 was provided with an incorrect status identifier, however, after careful reconsideration, it is noted that claim 8 does have the correct status identifier.

Information Disclosure Statement

Applicant's information disclosure statement filed May 31, 2007 is acknowledged. However, only the Abstract of WO 03/044188 has been considered since the remainder of the WO Document has not been translated in English. Accordingly, the Examiner has considered the information disclosure statement, and a signed copy is enclosed herewith.

Applicant's information disclosure statement filed November 2, 2006 is acknowledged. The submission is in compliance with the provisions of 37 CFR §1.97. Accordingly, the Examiner has considered the information disclosure statement, and a

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signed copy is enclosed herewith.

Applicant's information disclosure statement filed October 13, 2005 is acknowledged. However, only the Abstract of JP 08208687 has been considered since the remainder of the Japanese Document has not been translated in English. Accordingly, the Examiner has considered the information disclosure statement, and a signed copy is enclosed herewith.

Applicant's information disclosure statement filed July 22, 2004 is acknowledged. However, only the Abstracts of EP 1144623, WO 99/07409, WO 01/42443, WO 01/70944, WO 02/55692, WO 02/55693, WO 03/043989, and WO 03/043689 have been considered since the remainder of the EP and WO Documents have not been translated in English. Accordingly, the Examiner has considered the information disclosure statement, and a signed copy is enclosed herewith.

Priority

It is noted that the instant application is a continuation in part of PCT/US03/05022, filed February 20, 2003.

It is also noted that the instant application claims priority to a laundry list of U.S. Provisional Applications and pending U.S. Patent Applications. The reference should be updated to reflect applications for patents that are pending or that have been abandoned.

Applicant is reminded that the later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or

original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

It is noted the instant claims have been amended and are currently drawn to a chemically modified double stranded short interfering nucleic acid (siNA) molecule comprising a sense strand and an antisense strand, wherein the antisense strand is complementary to a vascular endothelial growth factor receptor 2 (VEGFr2) gene.

The instant application claims priority to a number of parent applications including U.S. Patent Application No. 10/306,747, filed November 27, 2002, and Provisional Applications 60/358,580, 60/363,124, and 60/386,782, filed February 20, 2002, March 11, 2002, and June 6, 2002, respectively. Now then, referring to U.S. Patent Application No. 10/306,747, it appears that this Application supports for the invention as instantly claimed.

Next then, referring to Provisional Applications 60/358,580, 60/386,782, and 60/363,124, it is noted that the Examiner cannot find support for the invention as instantly claimed. While it appears that the Provisional Applications have support for short interfering RNAs (siRNAs), the Applications do not support short interfering nucleic acid (siNA) molecules of the instant invention. In fact, it does not appear that Provisional Applications 60/358,580, 60/386,782, or 60/363,124 even recite the term, "short interfering nucleic acid (siNA) molecule".

In summary, Applicants claim priority to a number of parent applications, however, only U.S. Patent Application No. 10/306,747 appears to have support for a chemically modified double stranded short interfering nucleic acid (siNA) molecule comprising a sense strand and an antisense strand, wherein the antisense strand is complementary to a vascular endothelial growth factor receptor 2 (VEGFr2) gene as instantly claimed. While it appears that Provisional Applications 60/358,580, 60/386,782, and 60/363,124 have support for short interfering RNAs (siRNAs), these Applications do not appear to support short interfering nucleic acid (siNA) molecules as claimed in the instant invention. In this regard, the instant claims have been afforded priority to the filing date of U.S. Patent Application No. 10/306,747, filed November 27, 2002.

If Applicants believe that they are entitled to an earlier priority date, the Examiner urges Applicant to specifically point where support can be found for a chemically modified double stranded short interfering nucleic acid (siNA) molecule comprising a sense strand and an antisense strand, wherein the antisense strand is complementary to a vascular endothelial growth factor receptor 2 (VEGFr2) gene in any other applications Applicants claim priority to.

Drawings

The drawings filed on September 18, 2003 are acknowledged and have been accepted by the Examiner.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The subject matter of the instantly claimed invention is drawn to a chemically modified double stranded short interfering nucleic acid (siNA) molecule comprising a sense strand and an antisense strand, wherein the antisense strand is complementary to a vascular endothelial growth factor receptor 2 (VEGFr2) gene.

The specification teaches a series of VEGFr2 siNAs and target sequences to human VEGFr2 (Genbank Accession No. NM_002253.1). However, the specification and the prior art also teach dozens of different VEGFr2 genes (see, for example, Genbank Accession Nos. listed at pages 142-146 of the instant specification and GenBank Accession Nos. AF063658, NM_010612, and NM_013062). Neither the instant specification, nor the prior art describe siNA molecules targeted to other VEGFr2 genes, other than Genbank Accession No NM_002253.1.

At the outset it is noted that the rejected claims do not recite any sequence identifier relating to a VEGFr2 gene. This sequence is thus considered to be defined by

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its function (i.e. the activity of a VEGFr2 gene) rather than by any one specific structure. Accordingly, the claims embrace siNA molecules that down-regulates expression of any sequence of any VEGFr2 gene, or any such molecule with analogous VEGFr2 gene activity, known or yet to be discovered, along with any isoform or allele present within this species, or any variant, polymorphic or otherwise, that is within reasonable similarity from these families of proteins that retain VEGFr2 gene activity.

To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. Thus, an applicant complies with the written-description requirement by describing the invention, with all its claimed limitations, and by using such descriptive means as words, structures, Figures, diagrams, formulas, etc., that set forth the claimed invention. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical, structure/function correlation, methods of making the claimed product, and any combination thereof. The representative sample requirement may be satisfied by supplying structural or functional information, or a combination of both, such that one of skill in the art would be satisfied that applicants were in possession of the genus as claimed. Further, the size of the representative sample required is an inverse function of the unpredictability of the art.

See the January 5, 2001 (Vol. 66, No. 4, pages 1099-1111) Federal Register for

the Guidelines for Examination of Patent Applications Under the 35 USC 112 ¶ 1, "Written Description" Requirement. These guidelines state: "[T]o satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, Figures, diagrams, and formulas that fully set forth the claimed invention. Possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing that the invention was "ready for patenting" such as by the disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that applicant was in possession of the claimed invention.

Further, See MPEP § 2163, which states "[A] biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence."

In order to synthesize the siNA molecules that down-regulates expression of a VEGFr2 gene, one of skill would first need the sequence of the VEGFr2 gene in order to synthesize said siNA. However, one of skill in the art could not immediately envision the genus of said siNA molecules that down-regulates expression of a VEGFr2 gene

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from the disclosure of a series of siNA molecules targeted to only one such sequence, particularly in the absence of any teaching by way of structure or reference to active domains or regions. The genus is not immediately envisioned because the genus of siNA molecules is considered to include not only the VEGFr2F sequence of Genbank Accession No. NM_002253.1 as taught in the instant specification, but also any such molecule with analogous VEGFr2 activity, known or yet to be discovered, along with any isoform or allele present within this species, or any variant, polymorphic or otherwise, that is within reasonable similarity from these families of proteins that retain VEGFr2 activity. However, the distinguishing characteristics of the claimed genus are not considered to be described herein, or in the prior art. Thus, because one of skill in the art could not envision any siNA molecules that down-regulates expression of a VEGFr2 gene, other than Genbank Accession No. NM_002253.1, one of skill would not be convinced that applicants were in possession of any siNA molecules that down-regulates expression of a VEGFr2 gene sequences that are heretofore undescribed.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

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1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berard et al. (American Journal of Pathology, 1997 Vol. 150, No. 4:1315-1326), in view of Parrish et al. (Molecular Cell, Vol. 6, pp. 1077-1087, 2000, Applicant's Document No. 246 on the information disclosure statement filed July 22, 2004), Elbashir et al. (The EMBO Journal, Vol. 20, No. 23, pp. 6877-6888, 2001, Applicant's Document Number 114 on the information disclosure statement filed July 22, 2004), Matulic-Adamic et al. (US Patent No. 5,998,203), Cook et al. (US Patent No. 5,587,471), and Schmidt et al. (Nucleic Acids Research, 1996, Vol. 24, No. 4, pages 573-581).

The instant invention is drawn to a double-stranded short interfering nucleic acid (siNA) molecule that down-regulates expression of a vascular endothelial growth factor receptor 2 (VEGFr2) gene, wherein said siNA molecule comprises about 19 to about 21

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base pairs. The invention is further drawn to modifications to the siNA molecule, including 2'-O-methyl, 2'-deoxy-2'-fluoro, 2'-deoxy, phosphorothioate and deoxyabasic modifications and one or more of the purine nucleotides are 2'-O-methyl and one or more of the pyrimidines are 2'-deoxy-2'-fluoro, as well as to a composition comprising the siNA molecule and a pharmaceutically acceptable carrier or diluent. It is noted that the instant specification at pages 69 and 70 discloses, "By "VEGFr2" is meant, protein, peptide, or polypeptide receptor or a derivative thereof... having vascular endothelial growth factor receptor type 2 (kdr) activity".

Berard et al. teach a 15-mer antisense oligonucleotide targeted to the translation initiation codon of the KDR gene that down-regulates expression of a KDR gene (see page 1318, second column). It is noted that the antisense oligonucleotide taught by Berard et al. was mixed with lipofection diluted 200-fold in DMEM, which constitutes a pharmaceutically acceptable carrier or diluent.

Berard et al. do not teach a double-stranded short interfering nucleic acid (siNA) molecule that down-regulates expression of a vascular endothelial growth factor receptor 2 (VEGFr2) gene.

Parrish et al. teach modified double stranded siNA molecules as nucleic acid inhibitors of gene expression, which comprise a first nucleotide sequence with complementarity to a target and a second nucleotide sequence with complementarity to said first nucleotide sequence. It is noted that one or both strands comprise modifications. Each strand of the siNA molecules taught by Parrish et al. comprises about 21 nucleotides, more specifically 26 nucleotides. Parrish et al. teach that certain

modifications were well tolerated on the sense, but not the antisense strand, indicating that the two trigger strands have distinct roles in the interference process (see summary). Parrish et al. teach 2'-deoxy-2'-fluoro pyrimidine modifications in the sense or antisense strand (see Figure 5). The assays carried out by Parrish et al. utilize pharmaceutically acceptable diluents, such as water.

Elbashir et al. teach dsRNA duplexes as nucleic acid inhibitors, which consist of 21-23 nucleotides in length with 2 nt or 3' overhangs. Elbashir et al. teach 2'-deoxy and 2'-O-methyl modifications to one or both strands. Elbashir et al. teach that modifications are tolerated depending on the location in the duplex. Elbashir et al. teach that substitution of the 2 nt 3' overhangs by 2'-deoxynucleotides had no effect and even the replacement by two additional ribonucleotides by 2'-deoxyribonucleotides adjacent to the overhangs in the paired region produced significantly active siRNAs. Elbashir et al. teach 2'-deoxythymidines. Elbashir et al. teach an embodiment wherein the siRNA is blunt ended with 21 nucleotides base paired between duplex strands (see Figure 1F). Elbashir et al. teach complete substitution of one or both strands of the siRNA duplex, wherein the completely substituted duplex is considered to comprise no ribonucleotides. Elbashir et al. teach that a 5'-phosphate on the target-complementary strand of a siRNA duplex is required for siRNA function.

Matulic-Adamic et al. teach chemical modifications of double stranded nucleic acid structures (see Abstract). The double stranded nucleic acid RNA molecules of Matulic-Adamic et al. are taught to be targeted to virtually any RNA transcript and achieve efficient cleavage (see column 1) and to be sufficiently complementary to a

target sequence to allow cleavage. Matulic-Adamic et al. teach the incorporation of chemical modifications at the 5' and/or 3' ends of the double stranded nucleic acids to protect the enzymatic nucleic acids from exonuclease degradation, which improves the overall effectiveness of the nucleic acid, as well as facilitates uptake of the nucleic acid molecules (see column 2). Matulic-Adamic et al. teach base, sugar and/or phosphate modification, as well as terminal cap moieties at the 5'-cap, 3'-cap, or both. Specifically, 3'-phosphorothioates, inverted abasic moieties, and 2'-O-methyl modifications are utilized. Matulic-Adamic et al. teach 2'deoxy nucleotides and 2'-deoxy-2'-halogen nucleotides, wherein Br, CL and F are representative halogens (see column 3, for example). The modifications can be in one or both of the strands and can be modifications of different types within the same structure.

Cook et al. teach various conjugates and modifications that can be incorporated into oligonucleotide inhibitors to improve the pharmacokinetic properties of an oligonucleotide, including glyceryl (see columns 2 and 3).

Schmidt et al. teach hairpin RNA nucleic acid inhibitor comprising a sense and antisense region connected via a polynucleotide or non-polynucleotide linker (see Figure 3). Schmidt et al. teach that linkers increase hairpin RNA cleavage efficiencies (see page 575).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make a double-stranded short interfering nucleic acid (siNA) molecule that down-regulates expression of a vascular endothelial growth factor receptor 2 (VEGFr2) gene using the teachings of Berard et al., and following the

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methods and teachings of Parrish et al. and Elbashir et al. It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to further incorporate chemical modifications as taught by Elbashir et al., Parrish et al., and Matulic-Adamic et al. to the siNA to impart increased stability and functionality to the double stranded molecule.

One of ordinary skill in the art would have been motivated to make a double-stranded short interfering nucleic acid (siNA) molecule that down-regulates expression of a vascular endothelial growth factor receptor 2 (VEGFr2) gene since Berard et al. taught the design and use of a 15-mer antisense oligonucleotide targeted to the translation initiation codon of the KDR gene in down-regulating KDR gene expression and it is obvious to substitute one functional equivalent for another, particularly when they are to be used for the same purpose. See MPEP 2144.06. Further, one of ordinary skill in the art would have been motivated to make a double-stranded siNA molecule that down-regulates expression of a VEGFr2 gene since Berard et al. taught the design and use of a 15-mer antisense oligonucleotide targeted to the translation initiation codon of the KDR gene that down-regulates expression of a KDR gene and the substitution of one known element for another would have yielded predictable results at the time of the invention.

One of ordinary skill in the art would have been motivated to incorporate each of the above listed modifications within a siNA molecule that down-regulates expression of a VEGFr2 gene since such modifications were known to enhance the activity and increase resistance to nucleases of nucleic acid specific inhibitors of target gene

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expression. The modifications were each known in the art, as evidenced by the modified siRNA duplexes taught by Elbashir et al. and Parrish et al., hairpins taught by Schmidt et al., and modified oligonucleotides taught by Cook et al. One would be motivated to maximize a double stranded nucleic acid by incorporating each of the modifications that were known in the art. Elbashir et al. and Parrish et al. each teach combinations of modifications to duplexes and teach that different modifications are tolerated at different locations of the duplex. One of ordinary skill in the art would be motivated to test modifications that are known to benefit oligonucleotide delivery and apply each of them to a dsRNA duplex in order to optimize delivery of the duplex. It was well known in the art at the time of filing to incorporate one or more modifications, including 2'-O-methyl or 2'-deoxy-2-fluoro nucleotide modifications, into oligonucleotides, as evidenced by Elbashir et al., Matulic-Adamic et al., and Parrish et al. Elbashir et al. demonstrated both 2'-deoxy and 2'-O-methyl modifications of double stranded oligonucleotides at the time the invention was made. Matulic-Adamic et al. taught double stranded oligonucleotides comprising more than one specific type of modification. Additionally, Parrish et al. teach various modifications to double stranded duplexes and teach that different modifications are tolerated at different locations of the duplex. Elbashir et al. and Parrish et al. demonstrate the routine nature of testing various chemical modifications for optimization and stabilization of a double stranded duplex. The cited art demonstrates that the specific modifications were extensively described in the art. One of skill in the art would be motivated to test modifications that are known to benefit oligonucleotide delivery and apply each of them to a double

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stranded nucleic acid molecule in order to stabilize and optimize delivery of the nucleic acid.

One of ordinary skill in the art would have a reasonable expectation of success of making a modified a double-stranded short interfering nucleic acid (siNA) molecule that down-regulates expression of a vascular endothelial growth factor receptor 2 (VEGFr2) given that each of the modifications were known in the art at the time the invention was made to add benefits to oligonucleotides, such as increasing resistance to nucleases. One of ordinary skill in the art would expect for such modifications to benefit siNA duplexes, as each had shown to benefit either siRNA duplexes or other antisense oligonucleotide inhibitors such as antisense oligonucleotides or ribozymes. One of ordinary skill in the art would reasonably expect for polynucleotide or non-nucleotide linkers as taught by Schmidt et al. to benefit the instant invention since such linkers were known in the art at the time the invention was made to increase cleavage efficiency.

Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Terra C. Gibbs whose telephone number is 571-272-0758.

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The examiner can normally be reached on 9 am - 5 pm M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

tcg
December 23, 2007

/Terra Cotta Gibbs/